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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/717,140	ENGELHARDT ET AL.	
	Examiner	Art Unit	
	FRANK W. LU	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *91-123* is/are pending in the application.

4a) Of the above claim(s) *106 and 109* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *91-105,107,108 and 110-123* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11/18/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on April 19, 2007 has been entered. The claims pending in this application are claims 91-123 wherein claims 106 and 109 have been withdrawn due to species election mailed on May 12, 2006. Rejection and /or objection not reiterated from the previous office action are hereby withdrawn in view of applicant's amendment filed on April 19, 2007.

Information Disclosure Statement

2. Non-patent literatures 2-14 from the information disclosure statement filed on March 13, 2008 have been considered. However, since there are no publication dates for these non-patent literatures, these non-patent literatures cannot be put in the cover page of the patent if this instant application is issued. Therefore, these non-patent literatures in the 1449 form filed on March 13, 2008 have been struck through.

Drawings

3. The newly submitted Figures 8-15 have been accepted by the office.

Specification

4. The disclosure is objected to because of the following informalities: (1) although the amendments related to the specification filed on April 19, 2007 described that case 09/302,817 was filed on February 3, 1998, since the data from US Patent Office showed that case

09/302,817 was filed on April 16, 1999, applicant is required to provide data to support that case 09/302,817 was filed on February 3, 1998; and (2) although BRIEF DESCRIPTION OF THE DRAWINGS of the specification related to Figure 18 filed on April 19, 2007 describes IBI 31 plasmid (pIbI 31-BH5-2) (SEQ ID NOS:22-24) and BlueScript II plasmid construct (pBSII//HCV) (SEQ ID NOS:25-27), since pIbI 31-BH5-2 contains three different nucleotides while pIbI 31 pBSII//HCV contains three different nucleotides, it is unclear which nucleotide sequences in IBI 31 plasmid (pIbI 31-BH5-2) and BlueScript II plasmid construct (pBSII//HCV) correspond to which sequences from SEQ ID NOS:22-27.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Scope of Enablement

Claims 91-105, 107, 108, and 110-123 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making a protein- nucleic acid complex, does not reasonably provide enablement for producing a specific nucleic acid in a cell *in vivo* when any kind of conjugate recited in claims 91-105, 107, 108, and 110-123 is introduced into any kind of cell *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

Claims 91-105, 107, and 108 are drawn to a conjugate, which when introduced into a cell, produces a specific nucleic acid, said conjugate comprising a protein-nucleic acid construct that comprises: (i) at least one promoter; (ii) at least one segment of said specific nucleic acid comprising a sequence coding for a protein; and (iii) an RNA polymerase. Claims 110-118 are drawn to a conjugate, which when introduced into a cell, produces a specific nucleic acid, said conjugate comprising a protein-nucleic acid construct that comprises: (i) at least one promoter; (ii) at least one segment of said specific nucleic acid comprising a template for transcription; and (iii) an RNA polymerase. Claims 119-123 are drawn to a conjugate, which when introduced in a cell, produces a specific nucleic acid, said conjugate comprising a protein-nucleic acid construct that comprises: (i) at least one promoter; (ii) at least one single-stranded segment comprising a sequence complementary to a primer present in said cell; and a polymerase. The invention is a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The Breadth of The Claims

Claims 91-105, 107, and 108 encompass any kind of conjugate comprising a protein-nucleic acid construct that comprises at least one promoter, at least one segment of said specific nucleic acid comprising a sequence coding for a protein and any kind of RNA polymerase wherein, when said conjugate is introduced into a cell *in vivo*, the conjugate can produce a specific nucleic acid. Claims 110-118 encompass any kind of conjugate comprising a protein-nucleic acid construct that comprises at least one promoter, at least one segment of said specific nucleic acid comprising a template for transcription, and any kind of RNA polymerase wherein, when said conjugate is introduced into a cell *in vivo*, said conjugate produces a specific nucleic acid. Claims 119-123 encompass any kind of conjugate comprising a protein-nucleic acid construct that comprises at least one promoter, at least one single-stranded segment comprising a sequence complementary to a primer present in said cell and any kind of polymerase wherein, when said conjugate is introduced into a cell *in vivo*, the conjugate can produce a specific nucleic acid.

Working Examples

The specification provides working examples (see pages 43-63) for amplification of different DNAs and amplification from RNA template. The specification provides no working example for any kind of conjugate comprising a protein-nucleic acid construct that comprises at least one promoter, at least one segment of said specific nucleic acid comprising a sequence coding for a protein and any kind of RNA polymerase wherein, when said conjugate is introduced into a cell *in vivo*, the conjugate can produce a specific nucleic acid as recited in

claims 91-105, 107, and 108, any kind of conjugate comprising a protein-nucleic acid construct that comprises at least one promoter, at least one segment of said specific nucleic acid comprising a template for transcription, and any kind of RNA polymerase wherein, when said conjugate is introduced into a cell *in vivo*, produces a specific nucleic acid as recited in claims 110-118, and any kind of conjugate comprising a protein-nucleic acid construct that comprises at least one promoter, at least one single-stranded segment comprising a sequence complementary to a primer present in said cell and any kind of polymerase wherein, when said conjugate is introduced into a cell *in vivo*, the conjugate can produce a specific nucleic acid as recited in claims 119-123.

The Amount of Direction or Guidance Provided and The State of The Prior Art

Although the specification teaches a protein- nucleic acid complex formed by M13mp18 RF and DNA polymerase (see Example 3, pages 45 and 46), the specification does not provide a guidance to produce a specific nucleic acid in a cell *in vivo* when any kind of conjugate recited in claims 91-105, 107, 108, and 110-123 is introduced into any kind of cell *in vivo*. Furthermore, there is no experimental condition and/or experimental data in the specification to support the claimed invention. Although it is known in the art that T7 RNA polymerase RNA can be produced in a cell *in vitro* when a conjugate comprising a vector comprising T7 RNA polymerase gene and T7 promoter, and T7 RNA polymerase is introduced into a cell *in vitro* wherein T7 RNA polymerase gene is controlled by T7 promoter in the vector (see Wagner *et al.*, US Patent No. 5,591,601, see abstract, columns 2, 3, and 5), during the process of the prior art search, the examiner has not found any art which is related to produce a specific nucleic acid in a

cell *in vivo* when any kind of conjugate recited in claims 91-105, 107, 108, and 110-123 is introduced into any kind of cell *in vivo*.

Level of Skill in The Art, The Unpredictability of The Art, and The Quantity of Experimentation Necessary

While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether any kind of conjugate recited in claims 91-105, 107, 108, and 110-123 can be introduced into a cell *in vivo* and produce a specific nucleic acid.

A conjugate recited in claims 91-105, 107, and 108 is read as a conjugate comprising a protein-nucleic acid construct that comprises at least one promoter, at least one segment of said specific nucleic acid comprising a sequence coding for a protein and any kind of RNA polymerase wherein the at least one promoter and the at least one segment of said specific nucleic acid comprising a sequence coding for a protein are not inside of a vector and the RNA polymerase can be any kind of RNA polymerase and, when said conjugate is introduced into any kind of cell *in vivo*, the conjugate can produce a specific nucleic acid. First, since the at least one promoter and the at least one segment of said specific nucleic acid comprising a sequence coding for a protein are not inside of a vector, and the specification does not provide a guidance to introduce a conjugate comprising a protein-nucleic acid construct into a cell in human body, in view of the specification, it is unclear how said conjugate can be introduced into a cell *in vivo* such as a cell in human body. Second, even through we assume that the at least one promoter and the at least one segment of said specific nucleic acid comprising a sequence coding for a protein are inside of a vector and the at least one segment of said specific nucleic acid comprising a

sequence coding for a protein is controlled by the at least one promoter, since the claims do not require that the RNA polymerase is bacteriphage T7 RNA polymerase which is a RNA polymerase capable of carrying out transcription with high promoter specificity and efficiency without involvement of any cellular transcription factor (see page 2114, right column from Chen *et al.,* Nucleic Acids Research, 22, 2114-2120, 1994) and do not limit sources of the cell and RNA polymerase, and it is known that other RNA polymerase such as RNA polymerase II can function only in the presence of cellular transcription factors (see Shilatifard *et al.,* Annu. Rev. Biochem.,72, 693-715, 2003) and the mechanisms of RNA synthesis in prokaryotes and eukaryotes are totally different, it is unclear how, when said conjugate comprising any kind of eukaryotic RNA polymerase is introduced into a prokaryotic cell, the conjugate can produce a specific nucleic acid such as a RNA or how, when said conjugate comprising any kind of prokaryotic RNA polymerase is introduced into an eukaryotic cell, the conjugate can produce a specific nucleic acid such as a RNA.

A conjugate recited in claims 110-118 is read as a conjugate comprising a protein-nucleic acid construct that comprises at least one promoter, at least one segment of said specific nucleic acid comprising a template for transcription, and an RNA polymerase wherein the at least one promoter and the at least one segment of said specific nucleic acid comprising a template for transcription are not inside of a vector and the RNA polymerase can be any kind of RNA polymerase and, when said conjugate is introduced into a cell *in vivo* and can produce a specific nucleic acid. First, since the at least one promoter and the at least one segment of said specific nucleic acid comprising a template for transcription are not inside of a vector, and the specification does not provide a guidance to introduce a conjugate comprising a protein-nucleic

acid construct into a cell in human body, in view of the specification, it is unclear how said conjugate can be introduced into a cell *in vivo* such as a cell in human body. Second, even through we assume that the at least one promoter and the at least one segment of said specific nucleic acid comprising a template for transcription are inside of a vector and the at least one segment of said specific nucleic acid comprising a template for transcription is controlled by the at least one promoter, since the claims do not require that the RNA polymerase is bacteriphage T7 RNA polymerase which is a RNA polymerase capable of carrying out transcription with high promoter specificity and efficiency without involvement of any cellular transcription factor (see page 2114, right column from Chen *et al.,* Nucleic Acids Research, 22, 2114-2120, 1994) and do not limit sources of the cell and RNA polymerase, and it is known that other RNA polymerase such as RNA polymerase II can function only in the presence of cellular transcription factors (see Shilatifard *et al.,* Annu. Rev. Biochem.,72, 693-715, 2003) and the mechanisms of RNA synthesis in prokaryotes and eukaryotes are totally different, it is unclear how, when said conjugate comprising any kind of eukaryotic RNA polymerase is introduced into a prokaryotic cell, the conjugate can produce a specific nucleic acid such as a RNA or how, when said conjugate comprising any kind of prokaryotic RNA polymerase is introduced into an eukaryotic cell, the conjugate can produce a specific nucleic acid such as a RNA.

A conjugate recited in claims 119-123 is read as a conjugate comprising a protein-nucleic acid construct that comprises at least one promoter, at least one single-stranded segment comprising a sequence complementary to a primer present in said cell and a polymerase wherein, the at least one promoter and the at least one single-stranded segment comprising a sequence complementary to a primer present in said cell are not inside of a vector and the polymerase can

be any kind of polymerase such as DNA polymerase or RNA polymerase and, when said conjugate is introduced into a cell *in vivo*, the conjugate can produce a specific nucleic acid. First, since the at least one promoter and the at least one single-stranded segment comprising a sequence complementary to a primer present in said cell are not inside of a vector, and the specification does not provide a guidance to introduce a conjugate comprising a protein-nucleic acid construct into a cell in human body, in view of the specification, it is unclear how said conjugate can be introduced into a cell *in vivo* such as a cell in human body. Second, even through we assume that the at least one promoter and the at least one single-stranded segment comprising a sequence complementary to a primer present in said cell are inside of a vector and the at least one single-stranded segment comprising a sequence complementary to a primer present in said cell is controlled by the at least one promoter, since the claims do not require that the RNA polymerase is bacteriphage T7 RNA polymerase which is a RNA polymerase capable of carrying out transcription with high promoter specificity and efficiency without involvement of any cellular transcription factor (see page 2114, right column from Chen *et al.,* Nucleic Acids Research, 22, 2114-2120, 1994) and do not limit sources of the cell and RNA polymerase, and it is known that other RNA polymerase such as RNA polymerase II can function only in the presence of cellular transcription factors (see Shilatifard *et al.,* Annu. Rev. Biochem.,72, 693-715, 2003) and the mechanisms of RNA synthesis in prokaryotes and eukaryotes are totally different, it is unclear how, when said conjugate comprising any kind of eukaryotic RNA polymerase is introduced into a prokaryotic cell, the conjugate can produce a specific nucleic acid such as a RNA or how, when said conjugate comprising any kind of prokaryotic RNA polymerase is introduced into an eukaryotic cell, the conjugate can produce a specific nucleic

acid such as a RNA. Third, even through we assume that the at least one promoter and the at least one segment of said specific nucleic acid comprising a sequence complementary to a primer present in said cell are inside of a vector and the at least one segment of said specific nucleic acid comprising a sequence complementary to a primer present in said cell is controlled by the at least one promoter, since the specification and available art do not show that a protein-nucleic acid construct that comprises at least one promoter, at least one single-stranded segment comprising a sequence complementary to a primer present in said cell and a DNA polymerase or reverse transcriptase can produce a specific nucleic acid when the protein-nucleic acid construct is introduced into any kind of cells, it is unclear how the conjugate comprising a DNA polymerase or reverse transcriptase recited in claims 119-123 can produce a specific nucleic acid when it is introduced into a cell.

With above predictability, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether any kind of conjugate recited in claims 91-105, 107, 108, and 110-123 can be introduced into any kind of cell *in vivo* and produce a specific nucleic acid.

Conclusion

In the instant case, as discussed above, the level of unpredictability in the art is high, the specification provides one with no guidance that leads one to claimed methods. One of skill in the art cannot readily anticipate the effect of a change within the subject matter to which the claimed invention pertains. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of

any working examples related to the invention and the no teaching in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 91-93, 96-98, 101, 102, and 110-115 are rejected under 35 U.S.C. 102(e) as being anticipated by Wagner *et al.,* (US Patent No. 62,657, filed on May 14, 1993).

Regarding claims 91 and 92, Wagner *et al.,* teach a conjugate, which when introduced in a cell, produces a specific nucleic acid, said conjugate comprising a protein-nucleic acid construct that comprises: (i) at least one promoter (ie., T7 promoter); (ii) at least one segment of said specific nucleic acid comprising a sequence coding for a protein (ie., coding sequence of T7 RNA polymerase); and (iii) an RNA polymerase (ie., T7 RNA polymerase) as recited in claim 91 wherein said at least one promoter (i) comprises a cognate promoter for said RNA polymerase (iii) (ie., T7 promoter) as recited in claim 92 (see abstract, column 2, lines 37-67, column 3, lines 1-12, and column 5, lines 5-33).

Regarding claim 93, Wagner *et al.,* teach that said protein-nucleic acid construct comprises a double-stranded nucleic acid (ie., double stranded plasmid) as recited in claim 93 (see columns 12 and 13).

Regarding claims 96-98, Wagner *et al.,* teach that said sequence coding for a protein in said segment (ii) comprises a sequence for said RNA polymerase (iii) (ie., the coding sequence of T7 RNA polymerase) as recited in claim 96, said sequence coding for a protein in said segment (ii) comprises a protein other than said RNA polymerase (iii) (ie., the nucleotide sequence encoding a functional or reporter gene) as recited in claim 97, said sequence coding for a protein in said segment (ii) comprises a sequence for said RNA polymerase (ie., the coding sequence of T7 RNA polymerase) and a sequence for a protein other than said RNA polymerase (ie., the nucleotide sequence encoding a functional or reporter gene) as recited in claim 98 (see column 2, lines 37-67, column 3, lines 1-12, and column 5, lines 5-33).

Regarding claims 101 and 102, Wagner *et al.,* teach that said RNA polymerase (iii) comprises T7, T3, SP6 (ie., T7 promoter) or a combination thereof as recited in claim 101 and further comprising a sequence for a protein wherein said protein is transcribed from said second promoter (ie., the second T7 promoter) as recited in claim 102 (see Figure 1, column 2, lines 37-67, column 3, lines 1-12, and column 8, lines 1-14).

Regarding claim 110, Wagner *et al., et al.,* teach a conjugate, which when introduced in a cell, produces a specific nucleic acid, said conjugate comprising a protein-nucleic acid construct that comprises: (i) at least one promoter (ie., T7 promoter); (ii) at least one segment of said specific nucleic acid comprising a template for transcription (ie., the coding sequence of T7 RNA

polymerase); and (iii) an RNA polymerase (ie., T7 RNA polymerase) (see abstract, column 2, lines 37-67, column 3, lines 1-12, and column 5, lines 5-33).

Regarding claims 111-115, Wagner *et al.,* teach that said specific nucleic acid being produced comprises sense RNA (ie., T7 RNA polymerase RNA), antisense RNA transcripts (ie., antisense RNA) or a combination of both as recited in claim 111 and said sense RNA codes for a protein (ie., T7 RNA polymerase) as recited in claim 112, said protein coding sense RNA codes for said RNA polymerase (iii) (ie., T7 RNA polymerase) as recited in claim 113, said protein coding sense RNA codes for a protein other than said RNA polymerase (iii) (ie., the gene of interest such as luciferase) as recited in claim 114, and said protein coding sense RNA codes for said RNA polymerase (iii) and a protein other than said RNA polymerase (iii) (ie., the gene of interest such as luciferase) as recited in claim 115 (see claims 11-18 in columns 20 and 21).

Therefore, Wagner *et al.,* teach all limitations recited in claims 91-93, 96-98, 101, 102, and 110-115.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 94, 119, 120, 122, and 123 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wagner *et al.,* as applied to claims 91-93, 96-98, 101, 102, and 110-115 above, and further in view of Henikoff *et al.,* (US Patent No. 4,843,003, published on June 27, 1989).

The teachings of Wagner *et al.,* have been summarized previously, *supra.*

Wagner *et al.,* do not disclose that said protein-nucleic acid construct comprises a single-stranded nucleic acid as recited in claim 95 and a protein-nucleic acid construct comprising at least one single-stranded segment comprising a sequence complementary to a primer present in said cell as recited in claim 119. However, Wagner *et al.,* teach a conjugate, which when introduced in a cell, produces a specific nucleic acid, said conjugate comprising a protein-nucleic acid construct that comprises at least one promoter (ie., T7 promoter) and an RNA polymerase (ie., T7 RNA polymerase) as recited in claim 119 (see abstract, column 2, lines 37-67, column 3, lines 1-12, and column 5, lines 5-33).

Regarding claims 120, 122, and 123, Wagner *et al.,* teach that said polymerase comprises an RNA polymerase as recited in claim 120 (see abstract, column 2, lines 37-67, column 3, lines 1-12, and column 5, lines 5-33). Since Wagner *et al.,* teach claim 91, the at least one segment of said specific nucleic acid comprising a sequence coding for a protein (ie., the coding sequence of T7 RNA polymerase) taught by Wagner *et al.,* must have an ability to hybridize with a primer

comprising RNA as recited in claim 122 and said sequence codes for a protein as recited in claim 123.

Henikoff *et al.,* teach that a cloning vector can be either a single stranded or a double stranded (see column 6, lines 50-62).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made a conjugate comprising a single stranded nucleic acid construct as recited in claim 94 and a conjugate comprising a single stranded nucleic acid construct that comprises at least one promoter and at least one single-stranded segment comprising a sequence complementary to a primer present in said cell as recited in claim 119 using a single stranded cloning vector as a cloning vector in view of the prior art of Wagner *et al.,* and Henikoff *et al.*. One having ordinary skill in the art would have been motivated to do so because the simple substitution of one kind of cloning vector (ie., the cloning vector taught by Wagner *et al.,*) from another kind of cloning vector (ie., the cloning vector taught by Henikoff *et al.,*) during the process of making a conjugate comprising a single stranded nucleic acid construct as recited in claim 94 and a conjugate comprising a single stranded nucleic acid construct that comprises at least one promoter and at least one single-stranded segment comprising a sequence complementary to a primer present in said cell as recited in claim 119, in the absence of convincing evidence to the contrary, would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made since the cloning vector taught by Wagner *et al.,* and the cloning vector taught by Henikoff *et al.,* are used for the same purpose (ie., cloning nucleic acids) and are exchangeable (see Henikoff *et al.,* column 6, lines 50-62).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 91-105, 107, 108, and 110-123 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 6,986,985 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because an obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but examined claims in this instant application are not patentably distinct from the reference claims because the examined claims are either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). Although claims 91-105, 107, 108, and 110-123 in this instant application are not identical to claims 1-18 of U.S. Patent No. 6,986,985 B1, since the contents of U.S. Patent No. 6,986,985 B1 teach that: (1) the construct recited in claim 91 or 119 can be single stranded or double stranded or a partially single stranded nucleic acid as recited in claims 94, 95, and 119 (see column 15, second paragraph); (2) the protein in the conjugate comprises DNA polymerase or reverse transcriptase as recited in claims 103 and 121 (see column 15, second paragraph); (3) the nucleic acid construct in the conjugate comprises at least one chemically modified nucleotide or nucleotide analog as recited in claim 104 (see column 15, second paragraph); (4) said RNA polymerase is linked to said protein-nucleic acid construct by means of a covalent linkage as

recited in claim 105 (see column 4, lines 59-61); (5) said RNA polymerase is linked to said nucleic acid construct by means of a nucleic acid binding protein as recited in claim 107 wherein said nucleic acid binding protein comprises a repressor protein bound to an enzyme as recited in claim 108 (see column 15, lines 1-17); and (6) said primer comprises RNA as recited in claim 122 (see column 12, lines 46-56), claims 1-18 of U.S. Patent No. 6,986,985 B1 are directed to the same subject matter and fall entirely within the scope of claims 91-105, 107, 108, and 110-123 in this instant application. In other words, claims 91-105, 107, 108, and 110-123 in this instant application are anticipated by claims 1-18 of U.S. Patent No. 6,986,985 B1.

Response to Arguments

In page 22, fourth paragraph of applicant's remarks, applicant argues that "[C]laims 91-105, 107, 108, 110-121, and 123 have been rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 6,986,985 B1. As noted in the previous section, US Patent NO. 6,986,985 should not be as prior art since this patent and the instant application share the same priority date, January 13, 1994. In view of the above arguments, the obviousness-type double patenting rejections have been overcome. Therefore, Applicants respectfully request that the obviousness-type double patenting rejection be withdrawn".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection because the obviousness-type double patenting rejection is not based on whether U.S. Patent NO. 6,986,985 is a prior art or not. Applicant can overcome this rejection by filing a terminal disclaimer.

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. No claim is allowed.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

/Frank W Lu /
Primary Examiner, Art Unit 1634
May 16, 2008